Attorney Docket No. 9052.53 PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Gordon Rex Paterson Dougal
Serial No.: 09/529,210
Filed: July 24, 2000
For: ELECTROMAGNETIC RADIATION THERAPY

Group Art Unit: 3739
Examiner: Henry M. Johnson, III.

Date: April 15, 2003

Commissioner for Patents
Washington, DC 20231

DECLARATION OF DR. GORDON REX PATERSON DOUGAL UNDER 37 CFR §1.132

I, Dr. Gordon Rex Paterson Dougal, do hereby declare and say as follows:

1. I am the sole inventor on the above-referenced patent application and am familiar with the contents thereof. I have read and understood the Official Action mailed October 29, 2002 (the "Action"). I have also read and understood U.S. Patent Nos. 6,063,108 to Salansky et al. ("Salansky") and 5,527,350 to Grove ("Grove"), which are cited in the Action.

2. I received my first Medical Degree MB ChB from University of Rhodesia in 1980, my second medical degree LRCP, LRCS from Edinbrough in 1993, my Engineering degree B Sc Engineering (Electronic) in 1992 from the University of Natal, South Africa, specializing in Optics and waves, Quantum theory of laser design, Acoustics and Microwaves. From 1990 to 1992 Technical Director of Raylaser cc, South Africa, involved in research into the biological effects of visible light in the 600nm to 750nm range. Developed a treatment for herpes labialis using 660nm LEDs. Moved to United Kingdom in 1992. Commenced clinical trials in United Kingdom in 1995 evaluating the effect of 660nm LEDs in the treatment of herpes labialis. Appointed Technical Director Virulite Ltd. (UK) in 1997 responsible for the research into the biological effects of light in the red to near infrared region of the spectrum. Set up clinical trials to evaluate potential light sources. Whilst progressing the research into the therapeutic potential of light I gathered the necessary approved experience to receive formal accreditation from the Royal College of General Practitioners in 2000. All research in the 600nm to 1300nm region was carried out at the Occupational Health Department, North Tees Hospital, Stockton-on-Tees, under the impartial

supervision of Consultant Dr C English, results were analyzed by Professor Peter Kelly, Director of Medical Research, University of Teeside (co-author and medical statistician). Sunderland University, United Kingdom, 2002 to 2003. I have taken clinical lead in the development of the physiological response of cells to 1072nm & 1268nm light. The laboratory evidence supports the clinical findings that 1072nm & 1268nm light alter cell physiology, a phenomenon not occurring in other wavelengths, specifically not occurring at 660nm.

3. In the Action, the Examiner argues that the invention is allegedly taught by Salansky because it is allegedly capable of operation at the wavelengths in the claims using commercially available emitters. The Action states that transmittance data shows that 660 nm has a higher water transmittance than 1072 nm, and concludes that if transmittance of water is a primary factor, the 660 nm wavelength should be more effective. The Action then cites the absorption coefficients given in Grove.

4. I co-authored a paper, "A pilot study of treatment of herpes labialis with 1072 nm narrow waveband light;" G. Dougal & P. Kelly; Clinical and Experimental Dermatology, **26**, 149-154 (2001), which is attached hereto as Exhibit A. As discussed in Exhibit A, we hypothesized that tissue penetration would be influenced by light transmitted by water, which represents the major component of the human body. Examination of the transmission spectrum of the water molecule demonstrated a peak transmission of light with a wavelength of 1072 nm, as shown in Exhibit A, Figure 1.

5. As discussed in Exhibit A, the interventions compared were 1) a single 5 minute treatment of 1072 nm narrow waveband of light (NWBL) and 2) a five times daily topical acyclovir (antiviral cream) applied until the cold sore was reported to be cured. Sixty volunteer subjects were recruited, and the interventions were administered according to accepted randomized single blind controlled clinical experimental practice. The study demonstrates statistically significant evidence from the trial that patients treated with 1072 nm NWBL within thirty-six hours of onset of herpes labialis reported that their cold sores

healed in half the time (four days) compared with patients treated with conventional medication (eight days) in the form of acyclovir cream.

5. As shown in Exhibit A, Figure 1, the Examiner is correct that transmittance data shows that 660 nm has a higher water transmittance than 1072 nm. However, it has been discovered that radiation therapy at a wavelength of 1072 nm has unexpectedly positive results when compared to 660 nm light. In particular, the maximum bandwidth of each light source can be defined as a "bandpass filter effect" as described by the transmission spectrum of water between 980 nm and 1300 nm. The cited art fails to recognize that this phenomenon exists where water passes 1072 nm and 1268 nm light selectively in the near infrared spectrum and provides a bandstop filter for light at 980 and 1200 nm.

6. The Action states that Salansky in treating herpes using a wavelength of 660 nm achieved relief and dryness of lesions in one to two days, which is less time than the three days cited in the instant application using 1072 nm (Salansky, col. 38, line 4). Salansky merely gives an anecdotal example of one 48-year-old female patient suffering from frequent herpes simplex attacks on her lips. Salansky claims that the patient's lesions did not respond to conventional therapy and usually took from 9 to 15 days to heal. Salansky then reports that the patient experienced relief and the lesion became dry within one to two days after the first treatment with 660 nm light. Drying and crusting of the lesions does not constitute healing time as defined in the clinical trial – the day the crust falls off leaving uninterrupted skin at the site of the cold sore.

7. Upon review of Salansky, it is my opinion that the anecdotal evidence cited in Salansky cannot be compared to the double blind randomized controlled clinical trial of sixty volunteer subjects reported in Exhibit A. Anecdotal evidence is considered of little, if any, weight by experts in the field due to the lack of clinical controls, protocol and statistics. Moreover, the clinical trial discussed in Exhibit A compared the healing time of treatment with 1072 nm NWBL to conventional treatment using the antiviral acyclovir. Salansky apparently reports only the total healing time of a single patient. The Food and Drug

Administration defines credible information as "peer reviewed published literature, or other reliable information gathered during a trial". A single anecdotal case does not constitute credible information.

8. I conducted a separate single blind randomized controlled trial using the identical protocol reported in Exhibit A only using 660 nm NWBL instead of 1072 NWBL. The interventions compared were a single five-minute treatment of 660 nm light and a five times daily topical acyclovir applied until the cold sore was reported to be cured. The results of this trial are attached as Exhibit B. The results of trial did not demonstrate a therapeutic benefit of 660 nm NWBL compared to topical acyclovir. Unlike Salansky's anecdotal evidence, the results of the trial in Exhibit B can be compared with the results of the trial in Exhibit A because both are single blind randomized controlled clinical trials using identical protocol.

9. In view of the above, the results with respect to 1072 nm NWBL were unexpected. Although there is a peak in the transmission spectrum of the water molecule at a wavelength of 1072 nm, other portions of the spectrum (including 660 nm) demonstrate higher transmission than 1072 nm. Taken together, the two trials of Exhibits A and B compare the healing times of herpes simplex when treated with 1072 nm light and 660 nm light. The 1072 nm therapy shows improvement over conventional therapy, while the 660 nm therapy does not.

10. Based on the results with respect to 1072 nm NWBL, it is my opinion that favorable results may be achieved with wavelengths centered at, or about, 1268 nm because 1268 nm represents another peak in the transmission spectrum of the water molecule.

11. From a physiological view, electromagnetic radiation from the sun gives our planet life, the shorter wavelengths (300 – 400 nm) are used in photosynthesis, plants also absorb light in the 600 – 700 nm & 800 – 900 nm region, human and animal vision utilizes wavelengths between 300nm and 800nm. Until now the selective transmission of 1072nm and 1268nm light by water (clouds etc) has not been recognized to be of any significance.

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12. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Gordon Rex Paterson Dougal Date: April 21, 2003

Clinical Dermatology: Original Article

A pilot study of treatment of herpes labialis with 1072 nm narrow waveband light

G. Dougal and P. Kelly

Occupational Health Department, North Tees Hospital, Stockton-on-Tees, UK

Appendix C

Summary

A randomized prospective double-blind study was performed to compare the efficacy of a single 5 min 1072 nm narrow waveband light application against topical aciclovir applied five times daily in the treatment of herpes labialis. Treatment was initiated within 36 h of the onset of symptoms and the end point was defined as the day that the crust was discarded leaving an uninterrupted underlying skin at the site of the cold sore. The results demonstrated that a single 5 min light treatment significantly reduced cold sore healing time by 4 days; 1072 nm light healed cold sores in 4.3 ± 1.8 days (mean ± *SD*) as compared with aciclovir applied five times daily, 8.5 ± 3.0 days ($P < 0.0001$).

Background

Although infrared light is recognized as a treatment of musculo-skeletal disorders and indolent wounds, the evidence that it has therapeutic effect remains anecdotal. Indeed, until very recently the results of clinical trials exploring proposed therapeutic effects of infrared light had not been documented with meaningful statistical significance.[1–6] In 1999, however, Schindl and Neumann demonstrated that low intensity laser therapy is an effective nonthermic treatment for recurrent herpes simplex infection.[7]

In the laboratory various photobiological effects of infrared light have been explored, albeit dictated by the random commercial availability of predominately laser light sources.[8–13] These well-documented experiments have demonstrated unequivocally that selected wavelengths of infrared light have nonthermal photobiological effect. We were unable to find any evidence to suggest that these laboratory results had been correlated with the known anecdotal clinical therapeutic effects of infrared light.

We hypothesized that within the infrared spectrum there might be one or more narrow wavebands of light with therapeutic photobiological effect. As long ago as 1981 Anderson and Parrish[14] introduced the possibility of treating large tissue volumes with certain long wavelength photosensitisers within the optical window of skin, between 600 and 1300 nm. We reasoned that tissue penetration would be influenced by light transmitted by water, which represents the major component of the human body. Examination of the transmission spectrum of the water molecule demonstrated a peak transmission of light with a wavelength of 1072 nm (Fig. 1)..

For this study we decided to use a narrow waveband of light centred at 1072 nm using quantities of light which would not have thermal effect. (Terms: 1072 NWBL = light with a centre wavelength of 1072 nm and a bandwidth of ± 20 nm).

Cold sores appeared to be the obvious choice when searching for a clinical model to observe the effects of light therapy. They are known to be activated by exposure to ultraviolet light[15] and recurrence rates are known to be reduced by exposure to low intensity laser therapy. Approximately 20% of the world's population suffer from cold sores, providing within the community a potentially large number of patient volunteers to be recruited into clinical trials.

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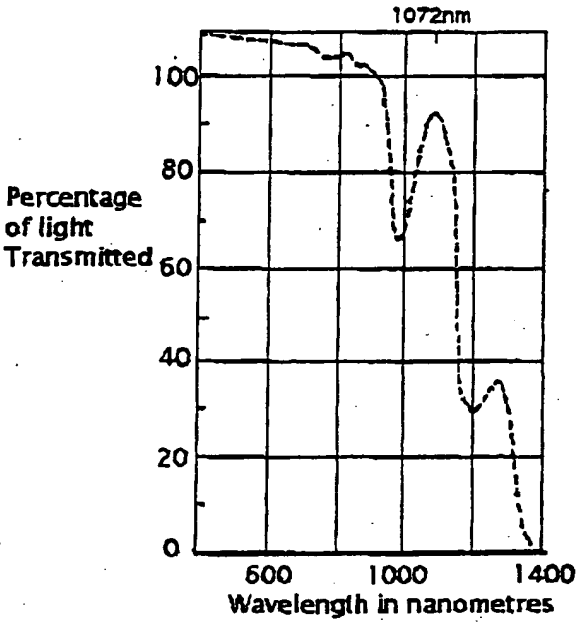

Figure 1 Light transmission spectrum of water between wavelengths 400 nm and 1400 nm.

Patients and methods

Protocol

Patient volunteers were recruited by advertisement within the local press after ethics permission had been obtained. Informed consent was obtained from all volunteer patients.

The interventions compared were a single 5 min treatment of 1072 NWBL vs. five times daily topical aciclovir applied until the cold sore was reported to be cured. Despite medical publications[16,17] to the contrary, topical aciclovir appears to be accepted by the general population as treatment of choice for cold sores. The duration of the cold sore must have been 36 h or less in all volunteers. The time of onset of the cold sore was defined as either the time of onset of symptoms or first appearance of the lesion, whichever was the soonest.

The initial parameters measured were cold sore size and the duration of the cold sore prior to intervention. Cold sore size was documented by photograph and the largest diameter measured by ruler.

The key outcome variable was the time at which the cold sore was cured, defined as the time when the crust had fallen off the cold sore leaving uninterrupted skin at the site. This was verified by the patient on a written response questionnaire and validated visually by an independent observer blind to treatment.

The possibility that using a light treatment device would have a placebo effect was explored by subdividing those patients receiving topical aciclovir into two groups: group 1 receiving only aciclovir and group 2 receiving aciclovir and placebo light. In a similar way any therapeutic effect of the placebo cream, advantageous or otherwise, was explored by treating half of the 1072 NWBL group with placebo cream.

The protocol was approved by North Tees General Hospital Ethics Committee.

Randomization method

The individuals were allocated to receive one of four treatments without restriction according to a standard computer-generated randomization table. Each treatment type was allocated an alphabetical letter which was assigned randomly to the patient number. Patient numbers were allocated sequentially. Each treatment arm was housed in a separate lettered container.

It was deemed unethical to withhold treatment from subjects, hence there is not a placebo control group in the study (i.e. either placebo light only or placebo cream only).

The 4 groups ran concurrently and were delivered the following treatments: group 1, topical aciclovir five times daily; group 2, topical aciclovir five times daily plus placebo light once for 5 min; group 3, 1072 NWBL once for 5 min; group 4, 1072 NWBL once for 5 min plus placebo cream five times daily.

Method of masking

The pharmaceutical creams were labelled with the patient number alone in Hartlepool General Hospital pharmacy. The pots in which the creams were dispensed were identical in external appearance and the quantity, consistency, colour and odour of the placebo cream appeared identical to topical aciclovir.

As the light is invisible to the human eye the external appearance of the light applicators and their external functions were identical. There was no mechanism by which either the patient or the researchers could discriminate between groups 2 and 4, and a separate staff member who independently followed-up the patients was blind to all four treatment arms. The code was located at Hartlepool General Hospital in a sealed envelope and was broken only at the conclusion of the trial after data analysis. The code was inaccessible to both the individuals carrying out the intervention and the outcome assessor who visually confirmed that the cold sore was healed. The

Table 1 Comparison of the four treatment groups.

	Patients treated between 18 and 36 h of onset of cold sore, % of total, (n)	Mean cold sore diameter [mm ± SD (n)]	Nurse observed cold sore cured [mean days ± SD (n)]	Patient reported cold sore cured [mean days ± SD (n)]
Light @1072 nm single 5 min application	8, 73% (11)	2.5 ± 1.1 (11)	7.0 ± 3.2 (11)	4.6 ±2.2 (11)
Light @1072 nm single application plus placebo cream five times daily	10, 71% (14)	3.3 ±1.9 (14)	8.7 ± 3.9 (9)	4.0 ± 1.4 (14)
Aciclovir cream five times daily	10, 71% (14)	3.3 ± 1.7 (14)	12.1 ± 4.3 (12)	8.8 ± 3.5 (14)
Aciclovir cream five times daily plus a single application of placebo light	11, 92% (12)	2.7 ± 1.0 (12)	10.6 ± 4.5 (12)	8.1 ± 2.5 (12)
P value	Lowest $P = 0.32$	$P = 0.45$	$P = 0.025$	$P < 0.0001$

data was analysed independently by The University of Teesside Medical Research Department prior to decoding.

Apparatus

The light source used a multimode laser diode array centred at 1072 nm with a bandwidth of ± 20 nm. The optical power was maintained between 5 and 10 mw/cm^2 peak power at the skin surface, switched at 600 hz with a 20% duty cycle. Internal monitoring of the light output ensured that treatment parameters remained constant. The treatment area was constant at 6 cm^2. The device, a class I laser product, operated from a 5 V double insulated supply with less than 20 μA earth leakage and contained an internal timer which facilitated a constant treatment time of 5 mins.

Statistics

Conventional one-way analysis of variance was used to compare cold sore size and days to heal among the four treatment groups. The two-sample *t*-test was used to compare the pooled aciclovir and 1072 NWBL groups.

For the proportion of patients treated between 18 and 36 h of onset, the four treatment groups were compared by applying the Fisher exact test to each pair of groups. This incurred three tests rather than six because the numbers from two of the groups were identical (Table 1). A single Fisher exact test was used to compare the pooled aciclovir and 1072 NWBL groups.

The statistical analysis was carried out using Minitab version 12.

Results

The data was analysed on an intention-to-treat basis.

Sixty volunteers were recruited into the trial. Eight patients were lost to follow-up and one patient with acne was excluded (Fig. 2). In the 1072 NWBL treatment group, 18 females and seven males were recruited and in the aciclovir treatment group, 22 females and four males were recruited. The mean age of

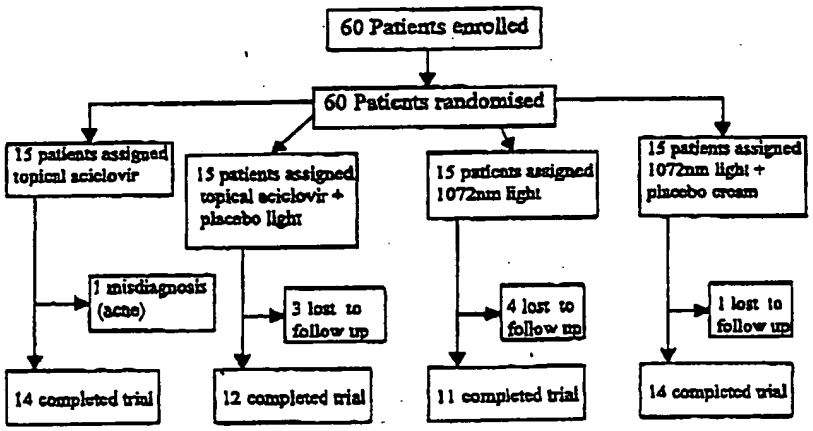

Figure 2 Trial profile.

Table 2 Pooled groups, active light vs. topical aciclovir

	Patients treated between 18 and 36 h of onset of cold sore, % of total, (n)	Mean cold sore diameter [mm ± SD (n)]	Nurse observed, cold sore cured [mean days ± SD (n)]	Patient reported cold sore cured [mean days ± SD (n)]
Active light, single 5 min treatment	18, 78% (25)	2.91 ± 1.53 (25)	7.8 ± 3.5 (20)	4.3 ± 1.8 (25)
Topical aciclovir five times daily	21, 87% (26)	3.0 ± 1.23 (26)	11.3 ± 4.3 (24)	8.5 ± 3.0 (26)
P value 95% confidence interval of the difference	$P = 0.46$	$P = 0.82$	$P = 0.005$ 1.1–6.0	$P < 0.0001$ 2.6–5.7

the 1072 NWBL treatment group was 41.8 years (range, 24–66 years) and the mean age of the aciclovir treated group was 40.3 years (range, 23–54 years).

Table 1 column 1 shows that the time interval between onset of symptoms and initiating treatment (less than 18 h or 18–36 h) was not significant between the groups ($P = 0.32$). Column 2 shows that the baseline parameter of cold sore size at the onset of treatment was not significantly different between the groups ($P = 0.45$).

Self reported time to cure

Table 1 column 4 shows the self-reported time to cure for each treatment arm. The two 1072 NWBL groups are reported as cured in about half the time than the two aciclovir groups, approximately 4 days vs. 8 days ($P < 0.0001$).

Table 2 is a comparison of the pooled 1072 NWBL groups vs. the pooled aciclovir groups. The results in column 4 compare the self-reported time to cure of the pooled groups and are also represented as a histogram in Fig. 3. The 1072 NWBL group is reported as healed in 4.3 days vs. 8.5 days in the aciclovir group ($P < 0.0001$).

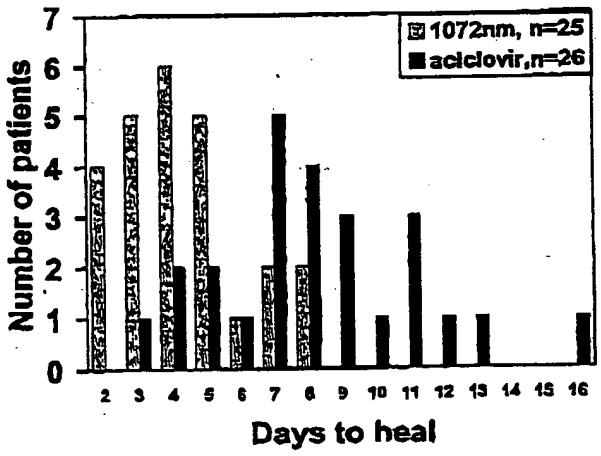

Figure 3 1072 nm light vs. aciclovir in the treatment of herpes labialis.

Once again there is no significant difference in the baseline parameters of cold sore size and the time of onset of treatment between the 1072 NWBL and aciclovir treated groups.

Nurse observed cold sore cured

The time at which the healed cold sore was available to be observed by the outcome assessor nurse was subject to a variable delay (Tables 1 and 2, column 3) affected by communication, transport and convenience.

However, the delays should have balanced out between the groups and there was no reason to suspect that any one group was seen sooner or later than the others. The results show a very similar pattern to those described for the self-reported time to cure, aciclovir 11.3 + 4.3 days, 1072 nm light 7.8 + 3.5 days, albeit with reduced statistical significance ($P = 0.005$).

Discussion

This study demonstrates statistically significant evidence from a randomized controlled trial that patients treated with 1072 NWBL within 36 h of onset of herpes labialis reported that their cold sores healed in half the time (4 days) compared with patients treated with conventional medication (8 days) in the form of aciclovir cream. To our knowledge this is the first time that a narrow waveband of light has been demonstrated to cause shortened cold sore healing time with a meaningful statistical significance. The difference in healing time was not influenced by the size of the cold sore. For both the 1072 NWBL and aciclovir treatment groups there was a placebo control for comparison and

all outcomes were recorded blind to the treatment received by the subject.

Previous research has shown that similar types of phototherapy using athermic quantities of low energy red or near infrared monochromatic light have been used for the acceleration of wound healing[18, 19] and in pain therapy.[20, 21] In addition it has been reported that this type of phototherapy might have an effect on several immunological reactions[22, 23] and is an effective treatment in preventing recurrent herpes simplex infection. *In vitro* investigations have not found any evidence to suggest that infrared irradiation inactivates the herpes simplex virus within infected cells.[24]

The mechanism by which infrared light has photobiological effect at molecular level, either demonstrated clinically, or by laboratory experiment, remains unexplained. We might imagine a hypothesis whereby cell membranes are the main beneficiary of light energy within the vicinity of 1072 nm. A more efficient cell membrane would increase resistance of the cell to virus entry, exposing the virus to an enhanced local immune response. Wound healing and repair might equally be enhanced.

In the light of our findings we would like to think that an increased awareness of the potential of infrared light to treat disease will stimulate further studies. Co-ordinated research would enable a map to be plotted of the therapeutic potential of light across the infrared spectrum. Of particular interest might be light within the optical window of skin (600–1300 nm) which would, in theory, have potential applications in the treatment of systemic disease processes. In the meantime we think that the knowledge that 1072 NWBL has therapeutic effect deserves further study, with respect to both dermatological and systemic disease.

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EXHIBIT B

660nm LEDs is ineffective in the treatment of cold sores

Summary

A single blind randomised controlled trial demonstrated that 660nm LEDs are ineffective in the treatment of cold sores.

Introduction

Over the years HeNe and semiconductor diode lasers[1] have been used with claimed therapeutic benefit in the treatment of cold sores, some have advocated the use of red light emitting diodes (LEDs) in the treatment of cold sores. A prospective single blind randomised controlled trial examines the efficacy of 660nm LEDs in the treatment of cold sores.

Patients and Methods

Protocol

Patient volunteers were recruited by advertisement within the local press. Informed consent was obtained from all volunteer patients.

Each light source produced the same optical power output of 5 - 10mw / sq cm microprocessor controlled to ensure that the light intensity remains constant.

.The interventions compared were a single 5-minute treatment of 660nm light versus 5 times daily topical aciclovir applied until the cold sore was reported to be cured. The duration of the cold sore must have been 36 hours or less in all volunteers. The time of onset of the cold sore was defined as either the time of onset of symptoms or first appearance of the lesion, whichever was the soonest.

The initial parameters measured were cold sore size and the duration of the cold sore prior to intervention. Cold sore size was documented by photograph and largest diameter.

The key outcome variable was the time at which the cold sore was cured, defined as the time when the crust had fallen off the cold sore leaving uninterrupted skin at the site. This was verified by the patient on a written response questionnaire and validated visually by an independent observer blind to treatment.

The possibility that using a light treatment device would have a placebo effect was explored by sub-dividing those patients receiving topical aciclovir into two groups: group 1 receiving only aciclovir and group 2 receiving aciclovir and placebo light. In a similar way any therapeutic effect of the placebo cream, advantageous or otherwise, was explored by treating half of the 660nm group with placebo cream.

North Tees General Hospital Ethics Committee approved the protocol.

Randomisation Method

The individuals were allocated to receive one of four treatments without restriction according to a standard computer generated randomisation table. Each treatment type was allocated an alphabetical letter that was assigned randomly to the patient number. Patient numbers were allocated sequentially. Each treatment arm was housed in a separate lettered container.

It was deemed unethical to withhold treatment from subjects and hence there is not a placebo control group in the study (i.e. either placebo light only or placebo cream only).

The 4 groups ran concurrently and were delivered the following treatments:

Group 1 Treated with topical aciclovir 5 times daily

Group 2 Treated with topical aciclovir 5 times daily plus placebo light once for 5 minutes

Group 3 Treated with active light once for 5 minutes

Group 4 Treated with active light once for 5 minutes plus placebo cream 5 times daily.

Method of Masking

The pharmaceutical creams were labelled with the patient number alone in Hartlepool General Hospital pharmacy. The pots in which the creams were dispensed were identical in external appearance and the quantity, consistency, colour and odour of the placebo cream appeared identical to topical aciclovir.

As the light is visible to the human eye blinding to the staff treating the volunteers was not possible. The device was shielded from the volunteers and placed against the skin and then activated, thus the patients were unaware of the light emissions. The external appearance of the light applicators and their external functions were identical. There was no mechanism by which the patient could discriminate between groups delivering aciclovir + placebo light and active light + placebo cream and a separate

staff member who independently followed up the patients was blind to all 4 treatment arms. The code was located at Hartlepool General Hospital in a sealed envelope and was only broken at the conclusion of the trial after data analysis. The code was inaccessible to both the individuals carrying out the intervention and the outcome assessor who visually confirmed that the cold sore was healed.

Apparatus

The 660nm $\pm$30nm utilised a LED array, the optical power was maintained at 5-10mw/sq cm at the skin surface. Internal monitoring of the light output in all devices ensured treatment parameters remained constant. The treatment area was constant at 6 cm^2. The devices operated from a 5-volt double insulated supply with less than 20 micro amps earth leakage and contained an internal timer that facilitated a constant treatment time of five minutes.

Statistics

Conventional one-way analysis of variance was used to compare cold sore size and days to heal among the four treatment groups. The two-sample t-test was used to compare the pooled aciclovir and 660nm groups.

For the proportion of patients treated between 18-36 hours of onset, applying the Fisher exact test to each pair of groups compared the four treatment groups. This incurred three tests rather than six because the numbers from two of the groups were identical (Table 1). A single Fisher exact test was used to compare the pooled aciclovir and 660nm groups.

Results

The data was analysed on an intention to treat basis.

Table 1.

	Patients treated between 18 – 36 hours of onset of cold sore, percentage of total, (n)	Mean cold sore diameter mm ± standard deviation, (n)	Nurse observed cold sore cured, mean days ± standard deviation, (n)	Patient reported cold sore cured, mean days ± standard deviation, (n)
Light @ 660nm single 5 min application	4 40% (10)	3.6 ±3.4 (10)	9.6 ±3.8 (10)	8.6 ±4.4 (10)
Light @ 660nm – single application plus placebo cream 5 times daily	3 30% (10)	2.8 ±1.54 (10)	9.3±3.6 (10)	8.2±3.7 (10)
Aciclovir cream 5 times daily	6 67% (9)	2.1 ±1.1 (9)	9.1±4.6 (9)	8.1±4.6 (9)
Aciclovir cream 5 times daily plus a single application placebo light	3 33% (10)	3.0 ±2.64 (10)	10.2 ±4.3 (9)	8.8±4.0 (10)
p-value		**p=0.**	**p=**	**p**

Table 2. Pooled groups, 660nm light vs aciclovir

	Patients treated between 18 – 36 hours of onset of cold sore, percentage of total, (n)	Mean cold sore diameter mm ± standard deviation, (n)	Nurse observed cold sore cured, mean days ± standard deviation, (n)	Patient reported cold sore cured, mean days ± standard deviation, (n)
Active light, a single 5 minute treatment	6 30% (20)	3.2 ±2.6 (20)	9.4 ±3.6 (20)	8.4 ±4.2 (20)
Topical aciclovir 5 times daily	9 50% (18)	2.55 ±2.0 (18)	9.7±4.2 (18)	8.6±3.8 (19)
p-value	**p=.**	**p=.**	**p=**	**p**

Discussion

Whilst red light[1] has been demonstrated to reduce recurrence of cold sores when used in higher power densities 660nm light from LEDs is ineffective in reducing cold sore healing time. Aciclovir has been demonstrated to be effective in the prodromal phase only, hence by the time treatment with topical acyclovir was initiated the period during which time it would have been effective had expired[2,3].

Whilst numbers are small, should there have been a marginal therapeutic benefit the numbers are sufficient to demonstrate a trend in that direction, this has not occurred.

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3. Spruance, Schipper et al. Early, patient initiated treatment of herpes labialis with topical 10% aciclovir- "Topical aciclovir was ineffective for the treatment of herpes labialis despite an optimum therapeutic opportunity" Antimicrobial agents and chemotherapy 1984 May:553.

4. Yu W, Naim JO, Lanzafame RJ. Effects of photostimulation on wound healing in diabetic mice. Lasers Surg Med 1997;20(1):56-63